

### **Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### **Listing of Claims**

1. (Currently Amended) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, where the reference sample and the measurement sample absorb light at each of selected wavelengths in a manner to produce similarly shaped spectra over the wavelengths measured, wherein the measurement sample has the spectral characteristics of an in vivo sample.

2. (Original) A reference sample as in claim 1, wherein the representative measurement sample includes multiple samples from multiple subjects.

3. (Original) A reference sample as in claim 2, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 30 or less when evaluated over the selected wavelengths measured.

4. (Original) The reference sample of claim 1, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200\text{ cm}^{-1}$  to  $7,200\text{ cm}^{-1}$ .

5. (Original) The reference sample of claim 1, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440\text{ cm}^{-1}$  to  $4,800\text{ cm}^{-1}$  and  $5,440\text{ cm}^{-1}$  to  $6,400\text{ cm}^{-1}$ .

6. (Original) The reference sample of claim 1, wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in wavenumbers

( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

7. (Original) A reference sample as in claim 2, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 10 or less when evaluated over the selected wavelengths measured.

8. (Original) The reference sample of claim 3, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200 \text{ cm}^{-1}$  to  $7,200 \text{ cm}^{-1}$ .

9. (Original) The reference sample of claim 3, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440 \text{ cm}^{-1}$  to  $4,800 \text{ cm}^{-1}$  and  $5,440 \text{ cm}^{-1}$  to  $6,400 \text{ cm}^{-1}$ .

10. (Original) The reference sample of claim 3, wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in wavenumbers ( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

11. (Original) A reference sample as in claim 2, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 1 or less when evaluated over the selected wavelengths measured.

12. (Original) The reference sample of claim 11, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200\text{ cm}^{-1}$  to  $7,200\text{ cm}^{-1}$ .

13. (Original) The reference sample of claim 11, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440\text{ cm}^{-1}$  to  $4,800\text{ cm}^{-1}$  and  $5,440\text{ cm}^{-1}$  to  $6,400\text{ cm}^{-1}$ .

14. (Original) The reference sample of claim 11 wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in wavenumbers ( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

15. (Original) A reference sample as in claim 2, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 30 or less.

16. (Original) A reference sample as in claim 2, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 10 or less.

17. (Original) A reference sample as in claim 2, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 1 or less.

18. (Original) A reference sample as in claim 1, wherein the representative measurement sample is from a single subject.

19. (Original) A reference sample as in claim 18, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 1500 or less when evaluated over the selected wavelengths measured.

20. (Original) The reference sample of claim 19, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200\text{ cm}^{-1}$  to  $7,200\text{ cm}^{-1}$ .

21. (Original) The reference sample of claim 19, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440\text{ cm}^{-1}$  to  $4,800\text{ cm}^{-1}$  and  $5,440\text{ cm}^{-1}$  to  $6,400\text{ cm}^{-1}$ .

22. (Original) The reference sample of claim 19, wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in wavenumbers ( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

23. (Original) A reference sample as in claim 18, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 1000 or less when evaluated over the selected wavelengths measured.

24. (Original) The reference sample of claim 23, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200\text{ cm}^{-1}$  to  $7,200\text{ cm}^{-1}$ .

25. (Original) The reference sample of claim 23, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440\text{ cm}^{-1}$  to  $4,800\text{ cm}^{-1}$  and  $5,440\text{ cm}^{-1}$  to  $6,400\text{ cm}^{-1}$ .

26. (Original) The reference sample of claim 23 wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in wavenumbers ( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

27. (Original) A reference sample as in claim 18, wherein the reference sample has a spectral similarity ratio, when compared with the representative measurement sample spectra, of 1 or less when evaluated over the selected wavelengths measured.

28. (Original) The reference sample of claim 27, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,200\text{ cm}^{-1}$  to  $7,200\text{ cm}^{-1}$ .

29. (Original) The reference sample of claim 27, wherein the measurement sample is tissue and the selected wavelengths measured is a spectral range of  $4,440\text{ cm}^{-1}$  to  $4,800\text{ cm}^{-1}$  and  $5,440\text{ cm}^{-1}$  to  $6,400\text{ cm}^{-1}$ .

30. (Original) The reference sample of claim 27 wherein the measurement sample is tissue, the analyte being measured is glucose and the selected wavelengths measured, in

wavenumbers ( $\text{cm}^{-1}$ ), are selected from the group consisting of: 4196, 4227, 4273, 4281, 4304, 4320, 4335, 4366, 4389, 4436, 4451, 4459, 4497, 4528, 4559, 4613, 4690, 4775, 4829, 4860, 4883, 4922, 5014, 5091, 5176, 5230, 5269, 5299, 5315, 5338, 5369, 5392, 5454, 5469, 5477, 5515, 5585, 5623, 5662, 5701, 5731, 5755, 5785, 5809, 5839, 5893, 5924, 5947, 6001, 6094, 6163, 6187, 6287, 6318, 6349, 6449, 6472, 6557, 6595, 6673, 6696, 6935, 6973, 7004, 7043, 7066, 7205, and combinations thereof.

31. (Original) A reference sample as in claim 18, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 4500 or less.

32. (Original) A reference sample as in claim 18, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 1500 or less.

33. (Original) A reference sample as in claim 18, wherein the reference sample has a regression weighted spectral similarity ratio, when compared to the representative measurement sample spectra, of 1 or less.

34. (Original) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, where the reference sample simulates the optical interaction between the measurement sample and the optical system.

35. (Original) A reference sample as in claim 34, wherein the reference sample has a spatial similarity, expressed in terms of standard deviation, of 0.079 or less.

36. (Original) A reference sample as in claim 34, wherein the reference sample has a spatial similarity, expressed in terms of standard deviation, of 0.052 or less.

37. (Original) A reference sample as in claim 34, wherein the reference sample has a spatial similarity, expressed in terms of standard deviation, of approximately 0.0.

38. (Original) A reference sample as in claim 34, wherein the reference sample has an angular similarity, expressed in terms of standard deviation, of 0.051 or less.

39. (Original) A reference sample as in claim 34, wherein the reference sample has an angular similarity, expressed in terms of standard deviation, of 0.036 or less.

40. (Original) A reference sample as in claim 34, wherein the reference sample has an angular similarity, expressed in terms of standard deviation, of approximately 0.0.

41-53. (Cancelled)

54. (Currently Amended) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, where the reference sample has the same primary optical absorber as the measurement sample, wherein the measurement sample has the spectral characteristics of an in vivo sample.

55. (Original) A reference sample as in claim 54, wherein the representative measurement sample contains first and second primary constituents, and wherein the reference sample contains the same first and second primary constituents.

56. (Original) A reference sample as in claim 55, wherein the second primary constituent comprises protein.

57. (Original) A reference sample as in claim 55, wherein the second primary constituent comprises lipid.

58. (Original) A reference sample as in claim 55, wherein the second primary constituent comprises a organic polymer.

59. (Original) A reference sample as in claim 54, wherein the measurement sample is tissue and the portion of the reference sample that is optically sampled contains less than 80% water by volume.

60. (Currently Amended) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, with the reference sample producing a non-stepwise reference spectrum that is optically similar to the representative measurement sample.

61. (Original) A reference sample as in claim 60, wherein the reference sample includes:  
an optically transparent layer;  
a diffusing layer; and  
a constituent layer disposed between the optically transparent layer and the diffusing layer.

62. (Original) A reference sample as in claim 61, wherein the representative measurement sample contains a primary constituent, and wherein the constituent layer contains the same primary constituent.

63. (Original) A reference sample as in claim 62, wherein the constituent layer contains water.



64. (Original) A reference sample as in claim 62, wherein the constituent layer contains protein.

65. (Original) A reference sample as in claim 62, wherein the constituent layer contains lipid.

66. (Original) A reference sample as in claim 61, wherein the diffusing layer is cone shaped.

67. (Original) A reference sample as in claim 61, wherein the optically transparent layer, the constituent layer, and the diffusing layer are cone shaped.

68. (Original) A reference sample as in claim 61, wherein the diffusing layer is non-planar.

69. (Withdrawn) A reference sample as in claim 62, wherein the optically transparent layer is flat.

70. (Withdrawn) A reference sample as in claim 60, wherein the reference sample includes:

- a container that is at least partially optically transparent; and
- a scattering solution in the container.

71. (Withdrawn) A reference sample as in claim 70, wherein the reference sample further includes a stirring mechanism for stirring the scattering solution.

72. (Withdrawn) A reference sample as in claim 70, wherein the scattering solution comprises reflective beads disposed in a constituent.

73. (Withdrawn) A reference sample as in claim 60, wherein the reference sample includes:

- a first optical splitting layer;
- a reflective layer; and
- a first constituent layer disposed between the first optical splitting layer and the reflective layer.

74. (Withdrawn) A reference sample as in claim 73, wherein the representative measurement sample contains a primary constituent, and wherein the first constituent layer contains the same primary constituent.

75. (Withdrawn) A reference sample as in claim 74, wherein the constituent layer contains water.

76. (Withdrawn) A reference sample as in claim 73, wherein the reference sample further includes:

- a second optical splitting layer; and
- a second constituent layer disposed between the first optical splitting layer and the second optical splitting layer.

77. (Withdrawn) A reference sample as in claim 55, wherein the reference sample includes:

- a container that is at least partially optically transparent;
- a constituent disposed in the container; and
- a spacer disposed in the container.

78. (Withdrawn) A reference sample as in claim 77, wherein the representative measurement sample contains a primary constituent, and wherein the constituent disposed in the container comprises the same primary constituent.

79. (Withdrawn) A reference sample as in claim 78, wherein the constituent disposed in the container comprises water.

80. (Withdrawn) A reference sample as in claim 77, wherein multiple spacers are disposed in the container.

81. (Original) A reference sample as in claim 60, wherein the reference sample includes:  
an optically transparent layer;  
a diffuse reflective layer disposed a distance from the optically transparent layer; and  
a constituent layer disposed between the optically transparent layer and the diffuse reflective layer.

82. (Original) A reference sample as in claim 81, wherein the representative measurement sample contains a primary constituent, and wherein the constituent layer comprises the same primary constituent.

83. (Original) A reference sample as in claim 81, wherein the constituent layer comprises water.

84. (Withdrawn) A reference layer as in claim 81, wherein the diffuse reflective layer is movable relative to the optically transparent layer to change the distance therebetween.

85. (Original) A reference sample as in claim 60, wherein the reference sample includes:  
a animal based bodily constituent.

86. (Original) A reference sample as in claim 85, wherein the animal based bodily constituent comprises animal bodily tissue.

87. (Original) A reference sample as in claim 85, wherein the animal based bodily constituent comprises animal bodily fluid.

88. (Withdrawn) A reference sample as in claim 60, wherein the reference sample includes:

a gel matrix;  
scattering media; and  
water.

89. (Withdrawn) A reference sample as in claim 88, wherein the gel matrix is placed in direct contact with the optical sampling device.

90. (Withdrawn) A reference sample as in claim 88, wherein the gel matrix is contained in a container that enables optical sampling.

91-102. (Cancelled)

103. (Original) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a test sample of interest, wherein the test sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, with the reference sample producing a reference sample spectrum that is similar to the test sample spectrum, the reference sample including a transmissive optical interface and an optical sampling compartment, the optical sampling compartment containing water and a diffusely reflective or scattering media.

104. (Original) A reference sample as in claim 103, wherein the reference sample spectrum has a spectral similarity ratio, when compared to a representative measurement sample spectra, of 30 or less.

105. (Original) A reference sample as in claim 103, wherein the reference sample spectrum has a regression weighted spectral similarity ratio, when compared to a representative measurement sample spectra, of 30 or less.

106. (Original) A reference sample as in claim 103, wherein the reference sample has a spatial similarity, expressed in terms of standard deviation, of 0.079 or less.

107. (Original) A reference sample as in claim 103, wherein the reference sample has an angular similarity, expressed in terms of standard deviation, of 0.051 or less.

108. (Withdrawn) A reference sample for maintaining prediction performance of an optical system used to measure an analyte or attribute in a representative measurement sample, wherein the representative measurement sample comprises a bodily tissue, bodily fluid or other biological sample containing the analyte or attribute, where the reference sample has a different primary optical absorber when compared to the measurement sample.

109. (Withdrawn) The reference sample of claim 108, wherein the spectral similarity is achieved by using at least one of the following: optical filters, absorbance filters, interference filters, or reflectance material.

110. (Previously Presented) A reference device for use with an optical system to maintain prediction performance of the optical system for a constituent of a representative measurement sample, the reference device comprising:

a reference material having a first optical similarity to the representative measurement sample; and

a structure for containing the reference material in a geometric configuration adapted to give the reference device a second optical similarity to the representative measurement sample;

wherein the second optical similarity is greater than the first optical similarity.

111. (Previously Presented) The reference device of claim 110, wherein the structure includes an optical interface allowing light to enter the reference device and interact with the reference material.

112. (Previously Presented) The reference device of claim 111, wherein the structure includes a diffusing cone.

113. (Previously Presented) The reference device of claim 110, wherein the structure provides a geometric configuration such that light entering the reference device may interact with the reference material through several different pathlengths.